REMARKS

Restriction:

In the April 28, 2005 Office Action the Examiner required restriction to one of the following groups under 35 U.S.C. §121:

Group I: Claims 1-57, 97-115, and 116-117, drawn to neutralizing antibodies and to a method of making;

Group II: Claims 58-79, and 118, drawn to a method of neutralizing botulinum neurotoxin A (BoNT/A);

Group III: Claims 80-96, drawn to polypeptides.

In addition, the Examiner required election of a species (sequence) from Tables 4, 9, or 11, and a single species (clone) from S25, C25, C39, 1C6, 1F3, 3D12, B4, huC25, Ar11, Ar2, WR1(V), WR1(T), 3-1, 3-8, 3-10, ING for initial examination.

In response to this restriction requirement, Applicants elect Group I, claims 1-57. 97-115, and 116-117.

With respect to the election of species, Applicant elect clone huC25 (SEQ ID NOS: 86 + 87 + 88 + 89 + 126 + 127 + 128 (VH) and SEQ ID NOs: 156 + 157 + 158 + 159 + 196 + 197 + 198 (VL)).

It is noted that the huC25 VH domain is a combination of SEQ ID NOS: 86-89 + 126-128, while the huC25 VL domain is a combination of SEQ ID NOS: 156-159 + 196-198.

With respect to the elected species, it is noted that claims 1, 3, 8, 17-57, 97, 99, 104, 113-117 read on the elected species.

Sequence Compliance.

The Examiner alleged that at page 8, lines 12 and 14, sequences which contain more than 4 amino acids are set forth that do not evidence a sequence identifier (SEQ ID NO). **In the preliminary amendment filed on April 12, 2004 (accompanying the sequence listing), page 8, lines 12 and 14 were amended to provide sequence identifiers.**

The Examiner alleged that Table 4 sets forth a plurality of amino acid sequencwes which must have sequence identifiers assigned and inserted. **In the preliminary amendment filed on April 12, 2004 (accompanying the sequence listing), a replacement Table 4 contaiing the required SEQ ID NOs was provided**. For the purposes of clarity, however, a clearer replacement Table 4 is provided herewith.

The Examiner alleged that at page 85, Table 11, clone huC25 is missing three SEQ iD NOs. **This row of Table 11 is carried over to page 86, where the SEQ ID Numbers are provided (see page 86, line 1).**

The Examiner alleged that at page 86, Table 11, clone huC25 is missing four SEQ iD NOs. **This row of Table 11 is carred over to page 87, where the SEQ ID Numbers are provided (see page 87, line 1).**

In view of the foregoing, Applicants believe the application is in compliance with the sequence listing rules.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3513.

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Table 4. Deduced protein sequences of VH and VL of BoNT/A Hc binding scFv classified by epitope recognized.

V_H Region			Framework 1 — CDR1 — Framework 2 — CDR2 — Framework 3 — CDR3 — Framework 4	SEQ. ID. NO.
Epitope	Clone	Lib		
1	C15	1	QVJLQQSGAELVRPGASVKLSCKTSGYSFT SYWMN WVKQGPGQGLEWIG MIHPSNSEIRFNQKFED MATLTVDKSSSTAYMQLSSPTSEDSAVYYCAR GIYYDYDGGNYYAMDY WGQGTTVTASS	48
	C9	1	----------N ----V----------V--	49
	ID5	2	E---VE----------N----A------ ----- ----R--------- --------T-L----K- K---------- -------E-Y--TL-- ------L-V--	50
	C1	1	----------A------ ----- ----R--------- -------DT-------- K------R-----IH---------- -L-GYGF WYFDV --------V--	51
	S25	1	----------A----L- ----- ----R--------- -----D-DT-------- K------T---------- -L-GNGF WYF-V --------V--	52
	1B6	2	--Q----------V---I---A---T-I D-A-H ----S-AKS----- V-SSYYGDTDY--I-KG K---------N----E-ARL--D---I----- RGKG ---- --------V--	53
	1C9	2	E-Q-K----------V---I---A---T-I D-AVH ----SHAKS----- V-STYYGDTDY-PK-KG K-----N---N----E-PRL------I----- RGKG ---- -----S--V--	54
	1E8	2	--Q-K----------V---I---A---T-I D-AW- -IR-F--KK---N- Y-S YSGSTGYNPSLKS RISI-R-T-KNQFFL--N-V-T--TGT----- -YD ---- -----S--V--	55
	1G7	2	--Q-K----------V---I---A---T-I D-AWY -IR-F--KK---N- Y-S YSGSTGYNPSLKS RISI-R-T-KNQFFL--N-V-T--TGT----- -YD ---- -----S--V--	56
2	1A1	2	EVKLVESGGGLVQPGGSRKLSCATSGFTFS DYYMS WIRQSPDKRLEWVA TISDGGTYTYYPDSVKG RFTISRDNAKNTLYLQMSSLKSEDTAMYYCVR HGYGNYPSH WYFDV WGAGTTVTVSS	57
	1F1	2	----------L-----A------ N-G-- -V--T--------- M--S--S-N--S----- -V--------S---------Q-------L-T- --------Y ----- ----------	58
	C39	1	Q-Q-Q-----S-K----L-----A------ ----- -V--T-E------- ------S---------- -V---------N----------I----- YR-DEGK -Y --Q--------	59
	C25	1	Q-Q-Q-------K----L-----A------ ----Y -V--T-E------- ------S---------- ----------N----------S- YR-DDAM -Y --Q--------	60
	2G5	2	----------K----L-----A------ S-A-- -V--T-E------- ----------T-N--- ----------HN------H----------A- NLPYDHV -Y --Q--S-----	61
	3C3	2	----K-------K----L-----A------ S-A-- -V--T-E------- ----------T-N--- ----------HN------H----------A- NLPYDHV -Y --Q--S-----	62
	3F4	2	EG----------K----L-----A------ S-A-- -V--T-EH------ -------F---T-N--- ----------HN------H----------A- NLPYDHV -Y --Q--S-----	63
	3H4	2	----------K---PL-----A------ S-A-- -V--T-EH------ -------F---T-N--- ----------HN------H----------A- NLPYDHV -Y --Q--S-----	64
3	1B3	2	EVQLQESGGGBVVQPGRSLRLSCAASGFTF SYAMH WVRQAPGKGLEWVA VISYDGSNKYYADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR DWSEGYYYYG MDV WGQGTTVIVSS	65
	1C6	2	QI--LQ---------- ----- ---------- ---------- ---------- ---------- --- ----------	66
	2B6	2	VKLVESGP-L-KPSQSLSLTCTVTGYSIT- D-AWN -I--F--NK---MG Y-N-----N-NP -L-N -ISIT--T---QFF-KL--VTS----T----- AGDGY-VD WYFDV --T--------	67

	1G5	2	Q----Q--AEL----A-VKM--K---Y--T --WTT --K-R--Q----IG D-YPGSGSTNYNEKF-S KA-LTV-T-SS-A-M-LS--TS--S------- ELGD A--Y -----S-----	68
	1H6	2	----------K--A-VKM--K---Y--T --WTT --K-R--Q----IG D-YP-SGSTNYNEKF-S KA-LTV-T-SS-A-M-LS--TS--S------- ELGD A--Y -----S-----	69
4	1F3	2	EVQLQQSGAELVKPGASVKLSCKASGYTFT SFWMH WVKQRPGRGLEWIG RLDPNSGETKYNEKFKS KATLTVDKPSSTAYMELSSLTSEDSAVYYCAR EAYGYWN FDV WGTGTTVTVSS	70
	2E8	2	---------- ----- ---------- ----------K---- ---------- ------- --- ----------	71
V_L Region			**Framework 1 _ CDR1 _ Framework 2 _ CDR2 _ Framework 3 _ CDR3 _ Framework 4**	
1	2C15	1	DIELTQSPAIMSASPGEKVIMTC SASS SVSHMY WYQQKPGSSPRLLIY DTSNLAS GVPIRFSGSGSGTSYSLTISRMEAEDSATYYC QQWSSYPFT FGSGTKLELKR	72
	C9	1	--D---------S-------I-- ---- ---Y-H -F-----T--KPW-- S------ ---A----------SV----A----- --Y-G--L- --A-----I--	73
	1D5	2	----------A--------I-- ----S I-S-NLH -----SETSPKPW-- G------ ---V----------S-----A----- --YG---L- --G-----I--	74
	C1	1	---------- ----- ----Y-- ---------- ------- ---V----------A----- -------L- --A--------	75
	S25	1	---------L-A--------I-- -V--S I-S-NLH -----S-T--KPW-- G------ ---V----------S-----A----- -------L- --A-----I--	76
	1B6	2	---------SLAV-L-QRA-IS- RA-ESVDSYGN-F-H -------QP-K---- RA---E- -I-A-------R-DFT--INPV--D-V----- --SNED-P- --A--------	77
	1C9	2	---------SLAV-L-QRA-IS- RA-ESVDSYGN-F-H -------QP-K---- RA---E- -I-A-------R-DFT---NPV--D-V----- --SNED-Y- --G-----I--	78
	1E8	2	---------- ---- ---Y-H -----S-T--KRW-- ---K--- ---A----------S-----A----- -----N-L- --A--------	79
	1G7	2	---------- ---- ---Y-H -----S-T--KRW-- ---K--- ---A----------S-----A----- -----N-L- --A--------	80
2	1A1	2	DIELTQSPASLAVSLGQRATISC RASESVDSYGNSFMH WYQQKPGQPPKLLTY LASNLES GVPARFSGSGSRTDFTLTIDFVEADDAATYYC QQNNEDPYT FGGGTKLEIKR	81
	1F1	2	--------T---------- ---------- ---------- ------- ---------- --------- ----------	82
	C39	1	----------R------ ----------H---- ---------- ------- ---- ---------- --------- ----------	83
	C25	1	---------- ----------H---Q ---------- R-----P -I----------G--------N-------V----- --S----F- --S--------	84
	2G5	2	---------IMSA-P-EKVTTT- S--S SV-Y-- -F-----TS-K-W-- ST---A- ----------G-SYS---SRM--E-------- --RSSY--- ----DQAGN-S	85
	3C3	2	---------IMSA-P-EKVTTT- ----------H---Q -F-----TS-K-W-- ST---A- ----------G-SYS---SRM--E-------- --RSSY--- ----DQAGN--	86
	3F4	2	-T--------IMSA-P-EKVTMT- S--S SV-Y-Y -------SS-R---- DT---A- ---V--------G-SYS---SRM--E-------- --WSSY-P- ----------	87
	3H4	2	---------IMSA-P-EKVTMT- ---S VSS-YL- -------SS-R---- DT---A- ---V--------G-SYS---SRM--E-------- --WSSY-P- ----------	88

3	1B3	2	DSELTQSPTTMAASPGEKITTTC SASSS ISSNYLH WYQQRPGFSPKLLIY RTSNLAS GVPARFSGSGSGTSYSLTIGTMEAEDVATYYC QQGSSIPRT FGGGTKLEIKR	89
	1C6	2	-I------ASL-V-L-RRA--S- R--E-VEYYGTSLMQ ----K--QP------ AA--VE- -------------DF--N=HPV-E -I-M-F- --SRKV-W- ----------	90
	2B6	2	YI------ASL-V-L-QRA--S- R--E-VDSYGNSFM- ----K--QP------ LA---E- ----------R-DFT---DPV--D-A----- --NNED-Y- ----------S	91
	1G5	2	-I------ASL-V-L-QRA--S- R--E-VEYYGTSLMQ ----K--QP------ AA--VE- -A----------DF--N-HPV-ED-I-M-F- --SRKV-Y- ----------	92
	1H6	2	-I------AI-S------V---- -V--- ---SN-- ----KS-T----W-- G------ ---V---------------SS-----A----- --W--Y-L- --A---V-LR-	93
4	1F3	2	DIELTQSPASMSASPGEKVTMTC RATSS VSSSYLH WYQQKSGASPKLWIY SASNLAS GVPSRFSGSGSGTSYSLTISSVEAEDAATYYC QQYIGYPYT FGGGTKLEIKR	94
	2E8	2	--------TT-A------I-I-- S-S-- IG-N--- -----P-F----L-- RT----- ---A---------------GAM----V----- --GSSI--- ----------	95